Acute Fatty Liver of Pregnancy Associated With Maternal and Fetal Metabolic Acidosis

Carl J. Werner, MD, Dennis P. Zoller, MD, William N. Baskin, MD, and Robert E. Eichmann, MD
St. Louis, Missouri, and Rockford, Illinois

Acute fatty liver of pregnancy (AFLP), also known as obstetric acute yellow atrophy, is a complication of the third trimester of pregnancy. Once thought to be rare and associated with a high fetal and maternal mortality (>70 percent), this disease has been reported more frequently and with much lower maternal and fetal mortality rates.[1-5] Through the use of laboratory studies, linked with a high index of suspicion, this entity is now being recognized before frank hepatic encephalopathy, renal failure, and fetal or maternal death occur.

The symptoms of AFLP usually begin after the 34th week of pregnancy. The initial symptoms, although nonspecific, may herald the onset of this sometimes fatal disease. These symptoms include nausea, vomiting, headache, malaise, and fatigue. Abdominal pain is frequently present either in the epigastric or right upper quadrant areas. The signs of AFLP are also nonspecific and may include scleral icterus, abdominal tenderness, or bleeding from venipuncture sites.

This report describes a case of AFLP with associated maternal and fetal metabolic acidosis. Although maternal acidosis has been reported as a complication of AFLP, it is infrequently recognized in the literature.[1-4,6-18] These reports cite decreased bicarbonate levels on serum electrolytes, but no therapy was given for the acidoses.

Both maternal acidosis and neonatal acidosis are amenable to recognition and therapy, and are therefore important in the supportive treatment of AFLP. In the case reported in this article, maternal acidosis was first indicated by hyperkalemia and decreased serum bicarbonate. Maternal arterial blood gas levels confirmed the presence of acidosis. After delivery of the infant, arterial blood gases were determined for the infant, which confirmed the presence of neonatal metabolic acidosis.

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From the Department of Family and Community Medicine, University of Illinois College of Medicine at Rockford, Rockford, Illinois. Requests for reprints should be addressed to Dr. Carl J. Werner, St. Anthony's Hospital, 10010 Kennerly Road, St. Louis, MO 63128.

CASE REPORT

A 21-year-old woman, gravida 1, para 0, presented to the labor and delivery department at 40 weeks' gestation complaining of intermittent vomiting for two weeks. Her prenatal course was uncomplicated, although she had "flu" at 36 weeks, followed by an upper respiratory tract infection. She was seen regularly during her pregnancy, was normotensive, and had normal findings on prenatal laboratory testing throughout. The only medications she took during her pregnancy were prenatal vitamins, iron sulfate, and an occasional acetaminophen. She discontinued birth control pills two months before becoming pregnant. Her blood type was O+. She smoked one pack of cigarettes per day, although she had an aversion to cigarettes for the 24 hours prior to presentation. This symptom, suggestive of liver disease, has been reported in one other case of AFLP.[16]

Examination at admission showed the patient had slightly icteric, somewhat sunken eyes. Her blood pressure was 130/80 mmHg, her pulse was 90/min, and she was afebrile. Findings on her chest examination were within normal limits. Her abdominal examination showed a gravid uterus, three finger breadths from the costal margin. The uterus was not tender. There was right upper quadrant tenderness near the liver, but the liver edge was not palpable. Her extremity examination showed no pedal edema. Pelvic examination revealed a cervix 2 cm dilated, 50 percent effaced, with the presenting part at +1 station. Urinalysis was negative for bilirubin, ketones, and protein. Initial laboratory data revealed a total protein of 50 g/L (5.0 g/dL), total bilirubin of 92 μmol/L (5.4 mg/dL), direct bilirubin 78 μmol/L (4.6 mg/dL), lactate dehydrogenase 7.22 μkat/L (434 U/L), gamma-glutamyltransferase 1.41 μkat/L (85 U/L), alkaline phosphatase 5.46 μkat/L (328 U/L), alanine aminotransferase 0.82 μkat/L (50 U/L), aspartate aminotransferase 3.71 μkat/L (223 U/L), blood urea nitrogen 12 mmol/L (34 mg/dL), serum creatinine 270 μmol/L (3.0 mg/dL), uric acid 700 μmol/L (11.8 mg/dL), and serum glucose 3.4 mmol/L (63 mg/dL). Amylase and lipase were within normal limits. Electrolytes revealed

a sodium level of 135 mmol/L (135 mEq/L), potassium 5.3 mmol/L (5.3 mEq/L), and a total carbon dioxide of 16 mmol/L (16 mEq/L).

The fetal monitor tracing showed a fetal heart rate of 140 beats per minute with good variability. Shortly after arriving in the labor department, the patient had an emesis of partially digested food. Fetal heart tones dropped to 70 beats per minute during this episode and remained there for 10 minutes. The patient was prepared for emergency cesarean section and taken to the operating room. A low transverse cesarean section was performed under general anesthesia, and a viable 2,670-g appropriate-for-gestational-age male infant was delivered with Apgar scores of 7 and 8. The mother's liver was normal in size and consistency and the gallbladder had no palpable stones during intraoperative palpation.

Initial infant laboratory assessment obtained 45 minutes after delivery by heel-stick showed a metabolic acidosis with a pH of 7.15, partial pressure carbon dioxide (PCO_2) 15.5 kPa (41 mmHg), partial pressure oxygen (PO_2) 8.5 kPa (64 mmHg), and total carbon dioxide 14.8 mmol/L (14.8 mEq/L). The infant's blood glucose level by heel-stick was 5.9 mmol/L (107 mg/dL). The infant received 2.5 mmol (2.5 mEq) of sodium bicarbonate through an umbilical artery catheter. Repeat arterial blood gases revealed a pH of 7.34, PCO_2 4.9 kPa (37 mmHg), PO_2 8.2 kPa (69 mmHg), and total carbon dioxide 20.6 mmol/L (20.6 mEq/L). The infant's hepatitis panel was negative for hepatitis B surface antigen and antibody, core antibody, and hepatitis A antibody. The infant's course was subsequently uneventful.

In the recovery room the mother was noted to have a profound metabolic acidosis with associated azotemia, hepatic failure, and coagulopathy despite the patient feeling quite normal. Laboratory results obtained in the recovery room showed a prothrombin time of 15.7 seconds and an activated partial thromboplastin time of 42.4 seconds. Her fibrinogen level was normal and her fibrin degradation products were 10 to 40 μg/mL. Her complete blood count showed 15.1 × 10^9/L (15,100/mm^3) white blood cells with 0.67 segmented cells, 0.15 band cells, 0.14 lymphocytes, and 0.4 monocytes. Her hemoglobin was 118 g/L (11.8 g/dL) with normal indices. Her platelet count was normal. Arterial blood gases were as follows: pH of 7.28, PCO_2 was 3.7 kPa (28 mmHg), PO_2 27.2 kPa (204 mmHg), total carbon dioxide 13.3 mmol/L (13.3 mEq/L) with fractional inspired oxygen concentration 0.40. Erythrocyte sedimentation rate was 8 mm/h. Her antinuclear antibody titer was negative. Serum ammonia was slightly elevated at 25 μmol/L (normal 5 to 20 μmol/L). She had an acetaminophen level of 0 μmol/L. At this point it was felt that the patient had acute fatty liver of pregnancy and was transferred to the intensive care unit for further observation and treatment.

The patient received 150 mEq (150 mmol) of sodium bicarbonate postoperatively and had normalization of arterial blood gases 12 hours after delivery. She received normal saline at a rate of 200 mL/h for the first 10 hours. She was given 10 mg of vitamin K subcutaneously every day and two units of fresh frozen plasma the first evening because of the prolonged prothrombin and partial thromboplastin times, but her prothrombin time did not become normal until six days postdelivery. The patient never showed signs of encephalopathy. The patient never had frank gastrointestinal bleeding but did have heme-positive stools postoperatively. She received ranitidine, 50 mg intravenously, every 12 hours in addition to intravenous cefazolin until sepsis was ruled out.

Twenty-four hours after delivery, the patient was noted to be slightly lethargic with a respiratory rate of 8/min, although her arterial blood gases showed no hypoxemia or hypercarbia. It was felt that the bradypnea was secondary to the accumulation of narcotics (given postoperatively) as a result of liver failure. Narcotics were subsequently withheld, and her respiratory rate returned to normal. Meperidine levels were not obtained.

The mother's blood test was negative for hepatitis B surface antigen and antibody, and negative for hepatitis A antibody. Liver biopsy was not performed because of the coagulopathy and the classical presentation of acute fatty liver of pregnancy. The mother and infant were discharged six days after delivery in good condition.

DISCUSSION

Acute fatty liver of pregnancy usually presents with nausea, vomiting, and icterus in the third trimester of pregnancy. The earliest reported case was at 28 weeks' gestation, although it usually presents in the 34th to 40th week of gestation. The diagnosis in this case was made on clinical grounds, specifically third trimester presentation with nausea, vomiting, icterus, and abdominal pain. Laboratory findings confirmed the diagnosis with an elevated prothrombin time and activated partial thromboplastin time, leukocytosis, decreased glucose level, elevated bilirubin, and moderately elevated serum glutamic-oxalocetic transaminase. A liver biopsy was contraindicated during the illness because of the coagulopathy[20] and was not performed later because of the classic presentation and rapid recovery.

Other causes of jaundice during pregnancy include viral hepatitis, toxemia of pregnancy, intrahepatic cholestasis, hemolytic uremic syndrome, acetaminophen toxicity, tetracycline toxicity, and chloroform toxicity. Chloroform and tetracycline toxicity occurred in years past when tet-

racycline was used for pyelonephritis during pregnancy and chloroform was used as an anesthetic agent.

Viral hepatitis was excluded in this case because there was only mild elevation of the amino transferase levels and no detectable antigens or antibodies. Benign jaundice of pregnancy (intrahepatic cholestasis) usually presents with elevated bilirubin also, but there is usually no coagulopathy or renal insufficiency as in this case. Toxemia of pregnancy was unlikely because of the absence of hypertension, proteinuria, and peripheral edema. Hemolytic uremic syndrome was unlikely without oliguria and in the presence of elevated direct bilirubin (hemolytic uremic syndrome usually presents with elevated indirect bilirubin) and liver failure. Acetaminophen toxicity was ruled out by the serum levels and the absence of significant ingestion history. Hemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome)[21] was unlikely because the patient did not have a low platelet count, had an abnormal prothrombin time and activated partial thromboplastin time, and had absence of a microangiopathic hemolytic anemia.

The laboratory findings in this case were characteristic of acute fatty liver of pregnancy with elevations of prothrombin time and activated partial thromboplastin time, blood urea nitrogen, creatinine, uric acid, transaminases, white blood cell count, and low blood glucose levels. The bilirubin levels in AFLP may initially be normal in the early part of the illness, but rise thereafter. The patient on presentation demonstrated elevated bilirubin levels.

Maternal and fetal mortalities were at one time thought to be near 75 percent each, but reports in the past six years have demonstrated a maternal and fetal mortality rate near 25 percent.[1,2,22] Lack of laboratory studies or liver biopsies in the past probably precluded identifying early or mild cases of AFLP. Most case reports in the past were from patients who had died, and the literature possibly reflected reporting only more severe cases.[2]

Other possible reasons for the dramatic decrease in mortality from AFLP could reflect early aggressive intervention, which was not common 20 years ago. In fact, many patients in the past remained with their infants undelivered for days in the hospital, only to succumb later to gastrointestinal bleeding, shock, or liver failure. Although it cannot be proved, it is thought by some authorities that early delivery is the safest approach for both the mother and infant.

The complications of AFLP are many and include liver failure with coagulopathy and encephalopathy, disseminated intravascular coagulation, upper gastrointestinal bleeding, ascites, pancreatitis, azotemia and renal failure, hypoglycemia, sepsis, postpartum hemorrhage with hypovolemia, pancreatitis with pseudocyst formation, seizures, shock, and death. Reported neonatal complications

of AFLP include hypoglycemia,[9] transient respiratory distress syndrome,[9,23] metabolic acidosis (two cases),[24,31] and fetal death.

Many fluid and electrolyte problems may be noted in the literature as complications of AFLP, including hypo- and hypernatremia,[1,8,16,25] hypo- and hyperkalemia,[1,8,14,16,18,25] metabolic acidosis,[1–4,6–18] and metabolic alkalosis.[8] Of 30 cases of metabolic acidosis reported in the literature as a complication of AFLP, only one was treated with bicarbonate (by mouth and by rectum in 1934 by Stander[17]) and many others were unrecognized. Normal acid-base status may also be found in AFLP.[7] The maternal acidosis is probably a reflection of volume depletion from repeated vomiting, anorexia, and upper gastrointestinal bleeding. Acute renal insufficiency, which is commonly seen in AFLP, may also contribute to the acidosis.[16,25–29] It seems logical that maternal acidosis causes fetal acidosis and could possibly contribute to fetal death. There are some reports of large maternal weight loss prior to delivery secondary to vomiting, and of tachycardia with decreased blood pressure, suggestive of volume depletion.[8,10,14,18,25,27–30]

In summary, this report suggests the need for more aggressive recognition of fluid and electrolyte abnormalities in cases of AFLP. Metabolic acidosis, metabolic alkalosis, hyponatremia, hypernatremia, hypokalemia, and hyperkalemia all may be seen. Metabolic acidosis should be treated with volume replacement as needed and sodium bicarbonate if severe. Many cases in the past ignored abnormalities of fluid balance and acid-base disturbances and their treatment. This report also suggests that postoperative narcotic use (morphine sulfate and meperidine) should be used judiciously in AFLP secondary to the possibility of accumulation with liver failure causing respiratory depression.

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